Remarks

Claims 1, 4, 10, 12, and 21-30 are pending and under consideration. With this Amendment, Claim 1 is being amended. No claims are being cancelled or newly added. Thus, after entry of this Amendment, claims 1, 4, 10, 12, and 21-30 are pending and under consideration. The amendments of the claims and the various rejections raised in the Office Action are discussed in more detail below.

I. The Amendments of the Claims

Claim 1 has been amended to replace the transitional phrase "consisting essentially of" to "comprising" following the preamble and to insert "consisting essentially of" with respect to the fusion protein. In addition, the term "having" has been deleted and replaced with "of" the specified SEQ ID NO. Support for the amendments can be found in the original claims and throughout the specification, such as on page 19, lines 27-35.

No new matter is added by virtue of the amendments. Entry of the amendment is respectfully requested.

II. Objections to Information Disclosure Statement

The Patent Office has objected to an Information Disclosure Statement (IDS) filed on January 12, 2004, and requests the expungement of the document. However, a review of the file shows that no IDS was filed by Applicant on that date. Examination of the electronic image file for this application in PAIR also shows that no such IDS was filed on the indicated date. Applicant did file IDSs on December 7, 2004 and June 14, 2006, and in both instances the references cited were within the subject matter of the pending application. In view of the foregoing, Applicant requests clarification of the IDS being objected to by the Patent Office.

III. Objections to the Specification

The specification is objected for non-compliance regarding use of trademarks in the disclosure. Specifically, the Patent Office contends that trademarks deleted in the previous response has not been replaced with generic definitions.

To comply with the provisions for use of trademarks in the specification, the trademark registration symbol "®" has been inserted and the specification amended to describe the product sold under the trademark. In support of the descriptions of the trademarked products, the product labels of the pharmaceutical AVASTIN and the ISOLEX device are provided in Exhibit A and Exhibit B, respectively.

In view of the foregoing, Applicant submits that the amendments to the specification comply with the provisions of M.P.E.P. § 608.01(v).

IV. Rejection Under 35 U.S.C. § 112, first paragraph: enablement

Claims 1, 4, 10 and 12 stand rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. In the rejection, the Patent Office contends that the instant claims still allow presence of other elements within the claimed composition which can materially affect the basic characteristics of the fusion protein used to activate the antigen presenting cells.

Without acquiescing to the position of the Patent Office, and in an effort to advance the prosecution of this case, Applicant has amended claim 1 to insert "consisting essentially of" preceding the phrase reciting the characteristics of the fusion protein and deleted "having" in relation to the specific portions of the fusion protein.

In view of the amendments, Applicant respectfully requests reconsideration and withdrawal of the rejections under the enablement clause of 35 U.S.C. § 112, first paragraph.

V. Rejection Under 35 U.S.C. § 102

Claims 1, 4, 10 and 12 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Small et al. 2000, *J. Clin. Oncol.* 18:3894-3903 ("Small") as evidenced by Ahmed et al., 2002, J. Pak. Med. Assoc. 52:54-56 ("Ahmed"). Applicant respectfully traverses the rejection.

A. Legal Standard

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); *see also* M.P.E.P. § 2131. The identical invention must be shown in as complete detail as it is contained

in the claim." *See Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

For a reference to anticipate by inherency, the claimed invention must necessarily or inevitably flow from the prior art. *See In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002); *see also Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377 [67 USPQ2d 1664] (Fed. Cir. 2003) ("The missing characteristic must be necessarily present, or inherent, in the single anticipating reference."). The fact that a certain result or characteristic *may* occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *See* M.P.E.P § 2112 (emphasis added); *see also In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993); *see also In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) ("The mere fact that a certain thing may result from a given set of circumstances is not sufficient.").

C. Claims are novel over Small and Ahmed

In rejecting the claims for anticipation by Small, the Patent Office states that a patient with a Gleason score of seven or less would be inherent to the population of patients described in Small.

Small describes phase I and phase II clinical trials using autologous dendritic cells exposed ex vivo to a recombinant fusion protein of prostatic acid phosphatase (PAP) linked to granulocyte macrophage colony stimulating factor GM-CSF). All patients enrolled in the study had hormone refractory prostate cancer (see Abstract and page 3895 under section "Patients") and an expected survival of at least 3 months, suggesting that many of the cancers had advanced and were not treatable with standard therapy (i.e., androgen deprivation). As noted in previous responses, Small is silent in regards to the Gleason score of the prostate cancer in the patient pool. Some patients, such as those in the phase I clinical trial, had metastatic disease in which the prostate cancer had spread to the bone and some soft tissues (see Small, Table I). The androgen-independent nature of the prostate cancer in all the patients, and the metastatic state of some of the prostate cancer patients indicates that many of the patients would likely have a Gleason score of greater than 7 (i.e., outside the scope of the instant claims).

Ahmed is proffered by the Patent Office to show that the patients in Small have a Gleason score within the scope of the instant claims. However, Ahmed concerns an examination of prostate biopsies to determine the incidence, i.e., occurrence, of prostate adenocarcinoma, and correlation of the presence of tumor with the Gleason scoring system. Ahmed does not address the Gleason score of the prostate cancer in the patients enrolled in the clinical trials described in Small, and therefore is not relevant to what is described in Small. As noted in the examination guidelines:

> Normally, only one reference should be used in making a rejection under 35 U.S.C. 102. However, a 35 U.S.C. 102 rejection over multiple references has been held to be proper when the extra references are cited to: . . . show that a characteristic not disclosed *in the reference is inherent*. . . .

See M.P.E.P § 2131.01 (emphasis added). The examination guidelines goes on to state:

> To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. *Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference* . . .

See id (emphasis added). Clearly, Ahmed is not a proper extrinsic evidence in support of anticipation by inherency since it does not address the nature (i.e., Gleason score) of the prostate cancers treated in Small.

Even assuming, *arguendo*, that Ahmed would be relevant to the patient pool in Small, an assumption that Applicant submits is not, Ahmed clearly states that the majority of tumours were moderate to "poorly differentiated", indicating that a significant number of prostate cancer had a Gleason score of greater than 7. If extrapolated to the study in Small, Ahmed would indicate that a significant number of patients in Small would have had a Gleason score of greater than 7.

As emphasized, anticipation by inherency requires that the claimed invention necessarily or inevitably flow from the prior art. Because Small does not describe the Gleason score of patients enrolled in the clinical trials, and Ahmed is not relevant in providing information on the patient pool in Small, there is no evidence to support the Patent Office position that the claimed

immunotherapeutic compositions were inherent in Small. Even if some the patients in Small were to have a Gleason score of 7 or less, the claimed subject matter would not necessarily and inevitably flow from the clinical trials in Small because of the likely presence of patients who had Gleason scores of greater than 7. In other words, dendritic cells prepared in Small *were not necessarily* and *inevitably* those of patients with prostate cancer with a Gleason score of 7 or less. The mere fact that some patients may have had prostate cancer with a Gleason score of 7 or less is not sufficient to establish inherency in this case.

The facts of instant case can be compared to those in *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 74 USPQ2d 1398 (Fed. Cir. 2005). In *SmithKline Beecham Corp. v. Apotex Corp.*, the patent at issue claimed paroxetine hydrochloride hemihydrate, a form of the drug marketed under the name "Paxil." The patent owner (SmithKline Beecham) initiated an infringement action against Apotex, a marketer of generic drugs. Apotex asserted that the patent was anticipated and invalid because of a prior art describing synthesis of paroxetine anhydrate. Although the asserted reference did not disclose paroxetine hemihydrate, Apotex contended that synthesis of the anhydrate inevitably forms the hemihydrate, i.e., arises as a natural derivative of the anhydrate. Both the patent owner and the infringer did not dispute the finding that manufacture of paroxetine anhydrate *inevitably* results in production of the hemihydrate and *that neither party could produce the anhydrate without producing the hemihydrate. See id* at 1344. Testing of the accused infringer's paroxetine anhydrate products also revealed the presence of the hemihydrate. *See id* at 1336. Consequently, the Federal Circuit held the claims anticipated and invalid based on inherency.

In contrast to the facts in *SmithKline Beecham Corp. v. Apotex Corp.*, each preparation of dendritic cells in Small does not necessarily or inevitably result in an immunotherapeutic composition of antigen presenting cells of the instant claims because there is nothing to show that *all patients* in Small had prostate cancer having a moderately to well differentiate cancer grade and a Gleason score of 7 or less. Thus, Small in view of Ahmed does not anticipate the claimed compositions. Accordingly, Applicant requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 102.

VI. Rejection Under 35 U.S.C. § 103(a)

Claims 1, 4, 10 and 12 stand rejected under 35 U.S.C. § 103(a) as being obvious over US Patent No. 6,210,662 to Laus et al. ("Laus") in view of Small et al. 2000, *J. Clin. Oncol.* 18:3894-3903 ("Small"), as evidenced by Ahmed et al. 2002, *J. Pak. Med. Assoc.* 52:54-56 ("Ahmed").

Claims 1, 4, 10 and 12 stand rejected under 35 U.S.C. § 103(a) as being obvious over US application publication No. 20040037843 by Fikes et al. ("Fikes") in view Small et al., 2000, *J. Clin. Oncol.* 18:3894-3903 ("Small") as evidenced by Ahmed et al. 2002, *J. Pak. Med. Assoc.* 52:54-56 ("Ahmed").

Applicant respectfully traverses each of the rejections.

A. The Present Claims

As summarized above, the present claims involve an immunotherapeutic composition, comprising activated, isolated antigen presenting cells (APCs), wherein the APCs are obtained from a patient diagnosed with prostate cancer having a moderate to well differentiated cancer grade and a Gleason score of 7 or less and wherein the APCs are stimulated by exposure ex vivo to a fusion protein consisting essentially of human prostatic acid phosphatase (huPAP) of SEQ ID NO:1 and human granulocyte-macrophage colony stimulating of SEQ ID. NO:3.

B. Cited References

Laus describes antigen presenting cell compositions stimulated with a protein complex of a dendritic cell binding protein and a polypeptide antigen. An exemplary protein complex is a fusion protein of GM-CSF and prostatic acid phosphate. Laus describes use of the protein complex for activating generally dendritic cells and other antigen presenting cells.

Small and Ahmed has been discussed above. To reiterate, Small describes clinical trials using dendritic cells stimulated using a fusion protein of GM-CSF and prostatic acid phosphatase while Ahmed describes a study examining the incidence of prostate carcinomas in a collection of prostate biopsies.

Fikes describes use of peptide epitopes for eliciting an immure response against tumor associated antigens. Peptide epitopes are chosen based on binding affinity to HLA complexes, with high affinity peptides correlating with greater immunogenecity. Fikes recites a number of epitopes of prostatic acid phosphatase, and possible uses to pulse dendritic cells.

C. Legal Standard Under 35 U.S.C. § 103(a)

Determining obviousness under 35 U.S.C. § 103(a) requires an objective analysis involving four factual inquiries, which include:

(a) determining the scope and content of the prior art,
(b) ascertaining the differences between the prior art and the claims in issue;
(c) resolving the level of ordinary skill in the art; and
(d) evaluating evidence of secondary considerations.

See Graham v. John Deere, 383 US 17, 18, 148 USPQ 459, 467 (1966); *see also* M.P.E.P. § 2141. A claim composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *See KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1385 (US 2007). It is also important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. *See id.* Thus, in assessing the scope and content of the prior art, the references must be considered in its entirety, *i.e.*, as a whole including portions that would lead away from the claimed invention. *See W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 US 851 (1984); *see also* M.P.E.P. § 2141.02.

Moreover, there must be a reasonable expectation of success. *See* M.P.E.P. § 2141. Hence, the obviousness analysis should consider whether the claimed invention is a predictable variation of the prior art elements. *See KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1385 (US 2007); *see also* M.P.E.P § 2141.

D. Claims are Non-Obvious Over Laus in view of Small and Ahmed.

Although Laus describes use of antigen presenting cells stimulated with a fusion protein of GM-CSF and prostatic acid phosphatase, Laus is a general description for use of protein

complexes to stimulate antigen presenting cells. The present claims are distinguished from Laus in requiring antigen presenting cells from a particular type of patient, i.e., an individual with prostate cancer having a moderate to well differentiated grade and a Gleason score of 7 or less. The general descriptions in Laus do not direct the skilled artisan regarding the benefits of using antigen presenting cells from a specified type of cancer patient.

Small does not add to the teachings or suggestions of Laus to prompt a skilled artisan to use dendritic cells from a particular type of patient because Small summarized the results of clinical trials involving patients in various stages of prostate cancer but without regard to the Gleason score and without providing any suggestion or guidance on the advantages of using antigen presenting cells from a particular type of patient. In fact, Applicant submits that Small is directed to treatment of advanced prostate cancer given the nature of patients in the clinical trials, namely, patients with androgen independent prostate cancer and advanced metastasis. Ahmed is not relevant to the obviousness determination since it does not address the types of patients in Small and is simply a study determining the incidence of prostate cancer in a collection of prostate biopsies.

Although the Patent Office advances an inherency argument to support its obviousness rejection, inherency under 35 U.S.C. § 103(c) would necessitate some recognition by those skilled in the art of the desirability of using dendritic cells from a particular type of prostate cancer patient since there must be some suggestion from the references or the common knowledge of the skilled artisan to combine the references, which contrasts with an assertion of inherency under 35 U.S.C. § 102. This is expressly provided in the examination guidelines:

> Obviousness cannot be predicated on what is *not* known at the time an invention is made, even if the inherency of a certain feature is later established.

See M.P.E.P. § 2141.02 (citing *In re Rijckaert*, 9 F.2d 1531, 28 USPQ2d 1955 (Fed. Cir. 1993)) (emphasis added). In the instant case, given the absence of any indication in the combination of Laus and Small that would suggest a benefit from using dendritic cells of a person with prostate cancer characterized by a moderate to well differentiated cancer grade and a Gleason score of 7 or less, and given the unpredictability in art regarding how certain cancers will

respond to cell based vaccines, the combination of Laus and Small would not prompt a skilled artisan to arrive at the claimed compositions.

In view of the foregoing, Applicant submits that Laus in view of Small and Ahmed does not establish a case *prima facie* obviousness. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 103.

E. Claims are Non-Obvious over Fikes in view of Small and Ahmed.

Fikes describes use of peptides containing specific epitopes to enhance the immune response against tumor associated antigens, including prostatic acid phosphatase. However, Fikes is absent any discussion or guidance regarding the types of patients from which antigen presenting cells for stimulation with the peptide epitopes. As discussed above, Small also does not address the types of patients from whom the immunotherapeutic compositions should be made to achieve an enhanced therapeutic benefit.

Consequently, the combination of Fikes and Small would merely prompt a skilled artisan to test a particular prostatic acid phosphatase epitope for use in the studies of Small, as opposed to use of antigen presenting cells from a particular type of prostate cancer patient. Ahmed is not relevant to the disclosure of Fikes and Small for the reasons stated above.

In view of the foregoing, Fikes in view of Small and Ahmed does not support a case of *prima facie* obviousness. Accordingly, Applicant respectfully requests reconsideration withdrawal of the rejections under 35 U.S.C. § 103.

VII. Conclusion

Claims 1, 4, 10, 12, and 21-30 are believed to satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly requested. Should any issues remain in the application and the Examiner believes that these issues can be resolved by a conference, the Examiner is encouraged to contact the undersigned representative at 650.838.4365.

No fees beyond those submitted herewith are believed to be due in connection with this Amendment. However, the Director is authorized to charge any additional fees that may

required, or credit any overpayment, to Perkins Coie LLP Deposit Account No. 50-2207 (**Order No. 57636-8127.US01**).

Respectfully submitted,
PERKINS COIE LLP

Date: October 22, 2007

/ Euk Oh /
Euk Charlie Oh
Reg. No. 54,345

Correspondence
Customer No. 28915
Tel: 650.838.4300
Fax: 650.838.4350